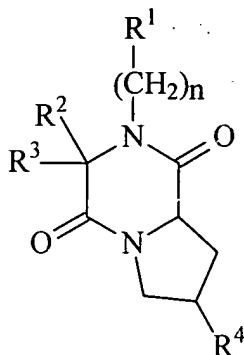


# CLAIMS

What is claimed is:

1. A compound of the structure (I):



(I)

and optical isomers, diastereomers, enantiomers and pharmaceutically acceptable salts thereof in isolation or mixture, where, independently at each location:

R<sup>1</sup> is an aryl or heteroaryl ring;

R<sup>2</sup> and R<sup>3</sup> are selected from hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring, and heterocycle aliphatic ring;

n is 1, 2 or 3;

R<sup>4</sup> is selected from -OR<sup>5</sup> and -NR<sup>6</sup>R<sup>7</sup>,

R<sup>5</sup> is selected from hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and heterocycle aliphatic ring; and

R<sup>6</sup> and R<sup>7</sup> are independently selected from hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and heterocycle aliphatic ring or R<sup>6</sup> and R<sup>7</sup> taken together with the nitrogen atom to which they are attached form a heterocycle aliphatic ring.

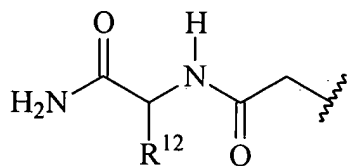
2. A compound of claim 1 wherein R<sup>1</sup> is phenyl and the phenyl is substituted with 1-4 substituents independently selected at each occurrence from alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring, heterocycle aliphatic ring.

3. A compound of claim 2 wherein  $R^1$  is phenyl having a substituent at the position *para* to the site of attachment to the piperazine ring.

4. A compound of claim 3 wherein  $R^1$  is phenyl having a substituent at the position *para* to the site of attachment to the piperazine ring, and the substituent has the formula  $R^{10}-R^9-R^8$ -, wherein  $R^8$  is selected from direct bond, alkylene and haloalkylene;  $R^9$  is selected from direct bond and carbonyl, and  $R^{10}$  is selected from hydrogen,  $R^{11}-O$ -,  $(R^{11})_2N$ - and  $R^{11}-(C=O)-NH$ -, wherein  $R^{11}$  is selected from hydrogen and organic groups having 1-20 carbons and optionally containing 1-4 heteroatoms selected from oxygen and nitrogen.

5. A compound of claim 4 wherein  $R^8$  is methylene;  $R^9$  is carbonyl, and  $R^{10}$  is  $(R^{11})_2N$ - wherein  $R^{11}$  is selected from hydrogen and organic groups having 1-20 carbons and optionally containing 1-4 heteroatoms selected from oxygen and nitrogen.


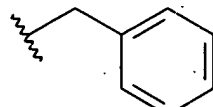
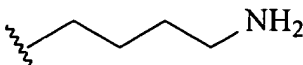
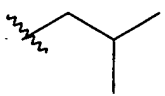
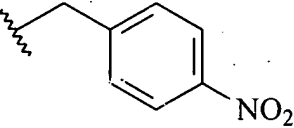
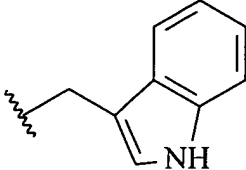
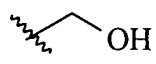
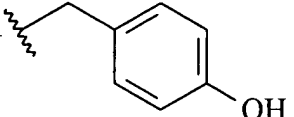
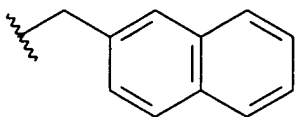
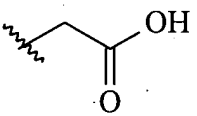
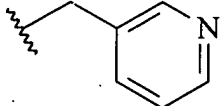
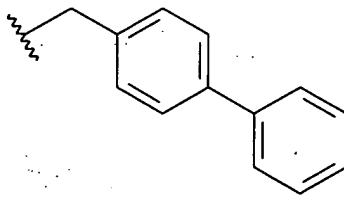
6. A compound of claim 3 wherein  $R^1$  is phenyl having a substituent at the position *para* to the site of attachment to the piperazine ring, and the substituent has the formula



1-20 carbons and optionally containing 1-4 heteroatoms selected from oxygen and nitrogen.

7. A compound of claim 6 wherein  $R^{12}$  is selected from hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and heterocycle aliphatic ring.

8. A compound of claim 7 wherein  $R^{12}$  is selected from

9. A compound of claim 1 wherein  $R^1$  is phenyl.

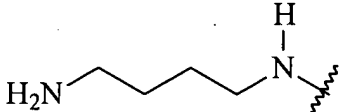
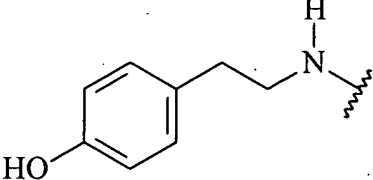
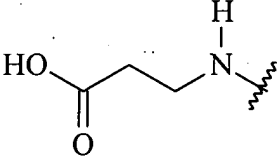
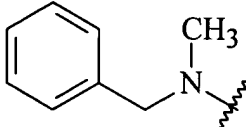
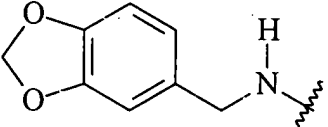
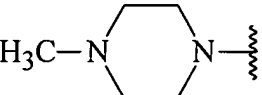
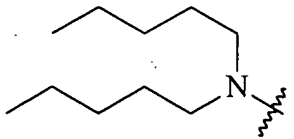
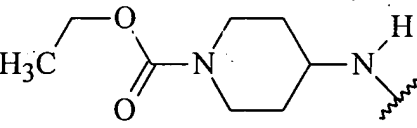
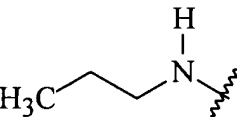
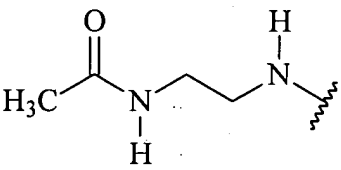
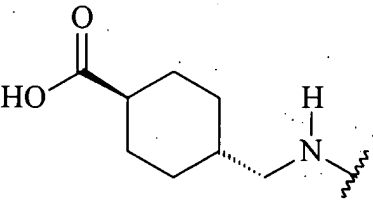
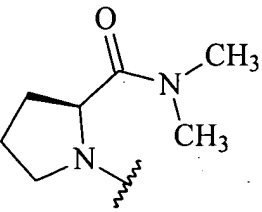
10. A compound of claim 1 wherein  $n$  is 1.

11. A compound of claim 1 wherein  $R^2$  and  $R^3$  are independently selected from groups of the formula  $R^{10}-R^9-R^8$ , wherein  $R^8$  is selected from direct bond, alkylene and haloalkylene;  $R^9$  is selected from direct bond and carbonyl, and  $R^{10}$  is selected from hydrogen,  $R^{11}-O-$ ,  $(R^{11})_2N-$  and  $R^{11}-(C=O)-NH-$ , wherein  $R^{11}$  is selected from hydrogen and organic groups having 1-20 carbons and optionally containing 1-4 heteroatoms selected from oxygen and

nitrogen, with the proviso that two  $R^{11}$  groups bonded to the same nitrogen may be bonded together so as to form a heterocyclic ring with the common nitrogen.

12. A compound of claim 11 wherein  $R^8$  is methylene;  $R^9$  is selected carbonyl, and  $R^{10}$  is  $(R^{11})_2N$ -

13. A compound of claim 12 wherein  $R^{10}$  is selected from:

14. A compound of claim 1 wherein  $R^4$  is  $-OR^5$ .

15. A compound of claim 9 wherein  $R^5$  is selected from hydrogen and alkyl.

16. A compound of claim 1 wherein  $R^4$  is  $-NR^6R^7$ .

17. A compound of claim 16 wherein  $R^6$  is hydrogen and  $R^7$  is  $R^{13}-C(=O)-$  where  $R^{13}$  is selected from:


18. A composition comprising a compound according to claim 1 and a pharmaceutically acceptable adjuvant, carrier, diluent or excipient.

19. A method of treating inflammation comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to claim 1.

20. A method for inhibiting a  $TNF-\alpha$  mediated processes, comprising administering to a patient in need thereof, through a therapeutically or prophylactically acceptable manner, a therapeutically or pharmaceutically effective amount of a composition comprising a compound of claim 1.

21. A method for inhibiting a  $TNF-\alpha$  mediated processes, comprising administering to a patient in need thereof, through a therapeutically or prophylactically acceptable manner, a therapeutically or pharmaceutically effective amount of a composition

comprising a compound of claim 1, wherein the administering is selected from transdermal, oral, intravenous, intramuscular, vaginal, rectal, pulmonary, subcutaneous, sublingual and transmucosal administration.

22. A method for inhibiting a TNF- $\alpha$  mediated processes, comprising administering to a patient in need thereof, through a therapeutically or prophylactically acceptable manner, a therapeutically or pharmaceutically effective amount of a composition comprising a compound of claim 1.

23. A method for treating a condition associated with an elevated level of NF $\kappa$ B activity in a subject, comprising administering to a subject in need thereof an amount of a compound effective to lower the NF $\kappa$ B activity, wherein the compound is a compound of claim 1.

24. A method for treating a condition associated with an elevated level of NF $\kappa$ B activity in a subject, comprising administering to a subject in need thereof an amount of a compound effective to lower the NF $\kappa$ B activity, wherein the compound is a compound of claim 1.

25. A method of inhibiting IL-8 production in a subject in need thereof comprising administering to the subject an effective amount of a compound of claim 1.

26. A method of inhibiting GRO- $\alpha$  production in a subject in need thereof comprising administering to the subject an effective amount of a compound of claim 1.

27. A method for inhibiting a CXCR1 and/or CXCR2 mediated processes, comprising administering to a patient in need thereof, through a therapeutically or prophylactically acceptable manner, a therapeutically or pharmaceutically effective amount of a composition comprising a compound of claim 1.

28. The method of claim 27 wherein the method inhibits a CXCR1 mediated processes.

29. The method of claim 27 wherein the method inhibits a CXCR2 mediated processes.

30. The method according to claim 27 wherein the administering is selected from transdermal, oral, intravenous, intramuscular, vaginal, rectal, pulmonary, subcutaneous, sublingual and transmucosal administration.

31. A method for treating an inflammation event, comprising administering to a patient in need thereof, through a therapeutically or prophylactically acceptable manner, a therapeutically or pharmaceutically effective amount of a composition comprising a compound of claim 1.

32. The method according to claim 31 wherein the administering is selected from transdermal, oral, intravenous, intramuscular, vaginal, rectal, pulmonary, subcutaneous, sublingual and transmucosal administration.

33. A method for identifying a binding partner to a compound of claim 1:  
immobilizing proteins known to be involved in the TNF- $\alpha$  signaling pathway onto a suitable carrier; and  
passing a solution of said compounds in isolation or mixture over said proteins and analyzing for compound:protein complex formation using surface plasmon resonance (SPR).

34. A method for identifying a binding partner to a compound of claim 1:  
providing said compound(s) bound to a solid support to provide solid phase  
compounds;  
contacting a cell or cell components with said solid phase compounds in isolation  
or mixture;  
removing uncomplexed cellular material, for example by gentle washing with  
aqueous buffer; and  
recovering said binding partner from the solid phase compounds.

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